

**BIODEGRADABLE MICROPARTICLES THAT STABILIZE AND CONTROL THE RELEASE
5 OF PROTEINS**

CLAIMS

We claim:

- 10 1. A controlled release formulation comprising: a protein mixed with a polysaccharide stabilizer and encapsulated in a biodegradable polymer.
2. The controlled release formulation according to claim 1, wherein the protein, stabilizer, and surfactant are encapsulated in the biodegradable polymer.
- 15 3. The controlled release formulation according to claim 1, wherein the biodegradable polymer comprises homo or heteropolymers of lactic and glycolic acids.
- 20 4. The controlled release formulation according to claim 1, wherein the biodegradable polymer is selected from the group consisting of hydrophobic bioabsorbable polymers such as polyglycolide, polylactide (D, L, DL), polydioxanones, polyestercarbonates, polyhydroxyalkonates, polycaprolactone (polylactones), polyethylene glycol, and copolymers thereof; preferably polyglycolide or polylactide, or a copolymer or polyglycolide-caprolactone of polyglycolide and polylactide, polylactide-polycaprolactone.
- 25 5. A controlled release formulation comprising:
 - a. a protein;
 - b. a stabilizer mixed with the protein; and
 - c. a surfactant coated on the stabilizer protein mixture.

6. The controlled release formulation according to claim 5, wherein the protein and stabilizer comprise microparticles and are coated with the surfactant.

7. The controlled release formulation according to claim 6, wherein the stabilizer has
5 a charge and the surfactant has a charge opposite to the stabilizer.

8. The controlled release formulation according to claim 5, wherein the stabilizer is uncharged and the surfactant is uncharged.

10 9. The controlled release formulation according to claim 5, wherein the stabilizer is uncharged and the surfactant is charged.

10. The controlled release formulation according to claim 5, wherein the protein and stabilizer are encapsulated in a biodegradable polymer.

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11. A controlled release formulation comprising:

- a. a protein;
- b. a stabilizer mixed with the protein; and
- c. a biodegradable polymer encapsulating the protein stabilizer mixture.

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12. A method for making stabilized protein particles comprising:

- a. providing a solution of protein;
- b. providing a solution of stabilizer;
- c. mixing the solutions; and
- d. generating microparticles from the mixture.

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13. The method according to claim 12, wherein the microparticles are generated by spray drying, lyophilization, electrohydrodynamic technology or other methods to create particles from solutions.

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14. The method according to claim 12, wherein the stabilizer is selected from the group consisting of polysaccharides, carrier proteins, and mixtures thereof.

15. The polysaccharides according to claim 14, wherein the polysaccharides are chosen from polysaccharide gums not limited to but including, guar gum, gum arabic, gum karaya, gum ghatti, locust bean gum, tamarind gum, carageenan gum, and pectin or mixtures thereof.

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16. The method according to claim 12, wherein when the stabilizer is a carrier protein, the stabilizer is selected from the group consisting of HSA, gelatin, BSA, and mixtures thereof.

10 17. The method according to claim 2, wherein the polymers are biodegradable polymers selected from the group consisting of hydrophobic bioabsorbable polymers such as polyglycolide, polylactide (D, L, DL), polydioxanones, polyestercarbonates, polyhydroxyalkonates, polycaprolactone (polylactones), polyethylene glycol and copolymers thereof;

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18. The method according to claim 2, wherein the polymers are biodegradable polymers that are selected from a group polymers that are sensitive to environmental conditions such as temperature or pH.

20 19. The method according to claim 18, wherein the polymers are block copolymers of polyethylene glycol and poly (lactic-co-glycolic) acid polymers.

20. The method according to claim 18, wherein the polymers are graft copolymers of polyethylene glycol and poly (lactic-co-glycolic) acid polymers.

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21. A method for making stabilized protein particles comprising:

- a. providing a solution of protein;
- b. providing a solution of stabilizer;
- c. mixing the solutions;
- 30 d. generating microparticles from the mixture; and
- e. coating the microparticles with surfactant.

22. A method for producing stabilized protein particles comprising:

- a. providing source of protein;

- b. providing a source of stabilizer;
- c. mixing the stabilizer and protein, wherein the ratio of stabilizer to protein is an amount effective for stabilizing the protein.

5 23. The method according to claim 22, wherein the stabilized protein particles are suspended in an organic solvent and coated with a surfactant in an organic solvent.

10 24. The method according to claim 22, wherein the organic solvent is selected from the group consisting of ethanol, dichloromethane, dimethyl sulfoxide, dimethyl formamide and mixtures thereof.

15 25. The method according to claim 22, wherein the protein and stabilizer are mixed in a ratio of stabilizer:protein of about 500:1 to about 1:1.

20 26. The method according to claim 22, wherein the protein and stabilizer are mixed in a ratio of stabilizer:protein of about 10,000:1 to about 50:1.

25 27. The method according to claim 22, wherein when the protein comprises a therapeutic protein, the protein and stabilizer are mixed in a ratio of stabilizer:protein of about 500:200 to about 1:1.

30 28. The method according to claim 22, wherein when the protein comprises a therapeutic protein, the protein and stabilizer are mixed in a ratio of stabilizer:protein of about 100,000:1 to about 1:1.

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